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Correlation of Thickened Endometrium on USG and Histopathological Spectrum in Perimenopausal and Post - Menopausal Women

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Abstract: ***Background: Abnormal uterine bleeding (AUB) is a bleeding pattern that differs in frequency, duration, and amount from a pattern observed during a normal menstrual cycle if bleeding occurs after menopause it is labelled as PMB. AUB can affect up to 50% of perimenopausal women. In India, the reported prevalence of AUB is around 17.9%. Aims & Objectives: To correlate the transvaginal ultrasound (TVUS) findings of endometrial thickness and histological patterns of the endometrium in order to evaluate the cause of PMB to correlate the transvaginal ultrasonographic (TVUS) findings of endometrial thickness and structural abnormality if any histopathological patterns of the endometrium. Materials & Methods: This is a prospective study comprised of 100 AUB women who are > 40 years of age in the peri and post - menopausal with PMB (Post - Menopausal Bleeding) attending the OPD. Clinical examinations of all the women were performed. After doing a TVUS analysis of the endometrial pattern and thickness, a D&C was performed. In perimenopausal women, the cut - off number for endometrial thickness was larger than 8 mm, perimenopausal despite prolonged heavy menstrual bleeding in women and ≥ 5 mm in postmenopausal women. All the tissue specimens were sent for histopathological examination. Results: 100 cases in total were reviewed, with 36% of them being menopausal and 64% of them being in the perimenopausal age range. Menorrhagia (54%) in perimenopausal women and PMB (34% in postmenopausal women) were reported to be the two most prevalent menstrual complaints. About 92% of the cases were multigravida. The most frequent uterine pathology found in 33% of cases was a fibroid uterus. In almost 53% of cases, the endometrial thickness was between 10 and 14.9 mm. Proliferative endometrium was the HPE result that was seen most frequently (37%), and endometrial malignancy was found in 2% of patients. Conclusion: Because of its practicality, accuracy, and non - invasiveness, TVUS should be the investigation of choice in perimenopausal women with AUB. A histological examination of the endometrium is necessary to rule out unusual alterations or endometrial cancer in individuals with endometrial thickness greater than 8 mm in perimenopausal despite prolonged heavy menstrual bleeding and 5 mm in postmenopausal women.***

Keywords: Abnormal uterine bleeding, PMB, TVUS, HPE

1. Introduction

Perimenopause is the phase preceding the onset of menopause, generally occurring around 40 years of age, during which the regular menstrual cycle of a woman changes from normal cycles to a pattern of irregular cycles. Menopausal transition includes a period of about 4–5 years before menopause, sometimes even several months, characterized by varying degrees of somatic and psychological changes that reflect the changes in the ovarian cycle. In some women, the most significant symptom is an irregular menstrual period, which must be carefully evaluated to determine whether it is the consequence of low oestrogen levels or an associated pathology[1].

Abnormal uterine bleeding (AUB) is one of the most common and challenging problems presented to the gynecologist[2]. It makes up to one - third of all outpatients presenting to Gynaecology OPD[3]. Any deviation in terms of the cycle, duration of bleeding, amount of blood loss, or a combination of all is called abnormal uterine bleeding[4]. AUB occurs in various forms, such as menorrhagia, polymenorrhoea, polymenorrhagia, post - coital bleeding, and postmenopausal bleeding[5]. The abnormal bleeding can be caused by a wide variety of disorders and may be a common presenting complaint in patients with a malignant or premalignant lesion[6].

AUB may be an expression of the hormonal milieu, or it could be the clinical presentation of benign or malignant lesions of the female genital tract in a perimenopausal woman. However, in the majority of cases, there are no structural abnormalities that can be seen, and this condition is known as dysfunctional uterine bleeding (DUB). Adenomyosis, DUB, and fibroid uterus are frequent hyper - oestrogenic disorders where the endometrium is still in the proliferative stage and may eventually develop into endometrial carcinoma if left untreated. In developing countries, cervical cancer is common due to a lack of screening programs. In order to determine the aetiological cause in a perimenopausal patient presenting with AUB and with the post - menopausal patient with post - menopausal bleeding.

Ultrasonography (transvaginal or abdominal) is a straightforward, non - invasive treatment that aids in the detection of any organic pathology as well as endometrial thickness[7]. It is well - accepted that various disease pathologies can be detected accurately by histopathological examination (HPE). Transvaginal Ultrasonography (TVUS) followed by dilation and curettage (D & C) in women

presenting with AUB helps in the detection of endometrial carcinoma, which is often preceded by endometrial hyperplasia[8]. Early detection of proper treatment of endometrial hyperplastic lesions is essential to prevent the progression to endometrial cancer[9, 10].

The goal of the current investigation was to compare the clinical manifestations in these instances with the results of the endometrial histopathology and ultrasonography.

2. Methods

This is a prospective study carried out from one month to the next at the Department of Gynecology and Obstetrics, AIMS, Bellur, Karnataka, India. The study comprised 100 women in total who reported having AUB and were 40 years of age or older. Once the study had received ethical approval, it was started. Patients provided thorough written informed consent. It was noted that there was a thorough history of menstrual abnormalities, length of complaints, obstetric, medical, and surgical history, as well as specifics of prior treatments received. Clinical evaluations were performed on all the women, including gynaecological, systemic, and gynaecological examinations and other relevant investigations were done.

All of these women underwent TVUS using the GE LOGIQ 500 MD MR3 ultrasonography system and a 7.5 MHz vaginal probe. The thickest part of the endometrium, which includes the outermost border of both sides of the endometrium, was measured as the maximal double - layer thickness in a midsagittal segment. In perimenopausal and postmenopausal women, the cut - off value for endometrial thickness was larger than 8 mm in perimenopausal despite prolonged heavy menstrual bleeding and ≥ 5 mm in postmenopausal women, respectively. All scans at the medical college were done by skilled sonologists. Within 24 to 48 hours of the TVUS, an inpatient treatment was scheduled that included a D&C and a histological examination (HPE) of the endometrium. Analysis of the histopathology report and the results showed a correlation between the endometrial thickness on TVUS and the menstrual irregularities. Statistical analysis was done using SPSS software package version 21. The Chi - square test was used to find the association of qualitative variables with the groups.

3. Results

The mean age of the subjects was 47.64 ± 8.556, with > 40 years of age as the inclusion criteria. Out of 100 subjects, 66 were in the age range of 40 to 50 years, followed by 25 in the age range of 51 to 60 years, 15 were in the range of 30 to 40 years, and 9 were between 61 to 70 years. The mean age of the menopause subjects was 56.08 ± 6.674, and the mean age of the menstruating subjects was 42.89 ± 5.161. (Table 1)

Table 1: Distribution of patients according to mean age, age groups, and mean age based on menstrual history

Distribution of patients based on mean age					
	N	Minimum	Maximum	Mean	SD
Age	100	40	70	57.64	8.56
Distribution of patients according to age group					
40 to 50 years		66		66.0	
51 to 60 years		25		25.0	
61 to 70 years		9		9.0	
Total		100		100.0	
Distribution of the patients according to mean age based on menstrual history					
Menstrual history	N	Minimum	Maximum	Mean	SD
Menopause	36	45	70	56.08	6.67
Menstruating	64	30	53	42.89	5.16

The majority of the patients (92%) were multigravida and 8% were nulli gravida. The Chi - square test showed no statistically significant association with parity ($\chi 2$=0.008, p=0.927). (Table 2)

Table 2: Distribution of patients according to parity and menstrual history

Parity		Menstrual history		Total
		Menopause	Menstruating	
Multi	Count	33	59	92
	%	91.7%	92.2%	92.0%
Nulli gravida	Count	3	5	8
	%	8.3%	7.8%	8.0%
Total	Count	36	64	100
	%	100.0%	100.0%	100.0%
Chi - square value - 0.008				
p - value - 0.927				

In the perimenopausal age range, 54% of patients had menorrhagia at the time of presentation, and 8% of patients had polymenorrhoea.34% had PMB in the postmenopausal age group, and 2 (5.6%) from each group had post - coital bleeding. There was a statistically significant association of presentation with menstrual history ($\chi 2$= 95.6, p=0.001). (Table 3)

Table 3: Distribution of patients according to presentation and menstrual history

Presentation		Menstrual history		Total
		Menopause	Menstruating	
Menorrhagia	Count	0	54	54
	%	0.0%	84.4%	54.0%
PMB	Count	34	0	34
	%	94.4%	0.0%	34.0%
Polymenorrhoea	Count	0	8	8
	%	0.0%	12.5%	8.0%
Post - coital bleeding	Count	2	2	4
	%	5.6%	3.1%	4.0%
Total	Count	36	64	100
	%	100.0%	100.0%	100.0%
Chi - square value - 95.6				
p - value - 0.001*				

*Significant

Table 4 shows the distribution of patients according to mean EM thickness based on menstrual history. Mean endometrium thickness (EM) thickness was higher in the

menstruating group (11.22 ± 3.03) as compared to the menopause group (10.58 ± 3.89).

Table 4: Distribution of patients according to mean EM thickness based on menstrual history

Menstrual history	N	Minimum	Maximum	Mean	SD
Menopause	36	4	18	10.58	3.89
Menstruating	64	5	19	11.22	3.03

TVUS examination revealed that 53% of patients had EM thickness in the range of 10 to 14.9, 32% of patients had EM thickness between 5 to 9.9, 14% of patients had EM thickness in the range of 15 to 19.9, and only 1% patient had EM thickness between 1 to 4.9. There was no statistically significant association between EM thickness and Menstrual history ($\varkappa 2$=0.008, p=0.927). (Table 5)

Table 5: Distribution of patients according to EM thickness and menstrual history

EM thickness		Menstrual history		Total
		Menopause	Menstruating	
1 to 4.9	Count	1	0	1
	%	2.8%	0.0%	1.0%
10 to 14.9	Count	15	38	53
	%	41.7%	59.4%	53.0%
15 to 19.9	Count	6	8	14
	%	16.7%	12.5%	14.0%
5 to 9.9	Count	14	18	32
	%	38.9%	28.1%	32.0%
Total	Count	36	64	100
	%	100.0%	100.0%	100.0%
Chi - square value - 0.008				
p - value - 0.927				

Evaluation of histopathological features and menstrual history found that the proliferative features were present in 37% of patients, about 8% in menopause patients, and 29% in menstruating patients. The secretive histopathological feature was seen in 25% of patients, polyp was seen in 19% of patients, atrophy was seen in 4% of patients in the menopause group, hyperplasia was seen in 7%, endometritis was present in 6%, EM cancer was seen in 2% of menopause patients. A statistically significant association with respect to proliferative features ($\varkappa 2$= 5.27, p=0.022) and atrophy features ($\varkappa 2$= 7.40, p=0.006) was observed. (Table 6)

Table 6: Distribution of patients according to histopathological features and menstrual history

Histopathological features			Menstrual history		Total	Chi - square value	p - value
			Menopause	Menstruating			
Proliferative	Absent	Count	28	35	63	5.27	0.022*
		%	77.8%	54.7%	63.0%		
	Present	Count	8	29	37		
		%	22.2%	45.3%	37.0%		
Secretive	Absent	Count	27	48	75	0.0	1.0
		%	75.0%	75.0%	75.0%		
	Present	Count	9	16	25		
		%	25.0%	25.0%	25.0%		
Polyp	Absent	Count	28	53	81	0.37	0.53
		%	77.8%	82.8%	81.0%		
	Present	Count	8	11	19		
		%	22.2%	17.2%	19.0%		
Atrophy	Absent	Count	32	64	96	7.40	0.006*
		%	88.9%	100.0%	96.0%		
	Present	Count	4	0	4		
		%	11.1%	0.0%	4.0%		
Hyperplasia	Absent	Count	33	60	93	0.15	0.69
		%	91.7%	93.8%	93.0%		
	Present	Count	3	4	7		
		%	8.3%	6.3%	7.0%		
Endometritis	Absent	Count	35	59	94	1.03	0.31
		%	97.2%	92.2%	94.0%		
	Present	Count	1	5	6		
		%	2.8%	7.8%	6.0%		
EM cancer	Absent	Count	34	64	98	3.62	0.06
		%	94.4%	100.0%	98.0%		
	Present	Count	2	0	2		
		%	5.6%	0.0%	2.0%		

Table 7 shows the cross - tabulation of histopathological features and EM thickness. Atrophy was present in 4% of patients; 1% of each had EM thickness between 1 to 4.9 and 10 to 14.9, and 2% of patients had EM thickness between 5 to 9.9. EM cancer was present in 2% of patients having a thickness of 15 to 19.9. A statistically significant association was found between atrophy and EM thickness ($\varkappa 2$= 25.62, p=0.001), EM cancer, and EM thickness ($\varkappa 2$=12.53, p=0.006).

Table 7: Distribution of patients according to histopathological features and TVUS of EM thickness

			EM thickness				Total	Chi - square value	p - value
			1 to 4.9	5 to 9.9	10 to 14.9	15 to 19.9			
Proliferative	Absent	Count	1	17	34	11	63	3.41	0.33
		%	100.0%	53.1%	64.2%	78.6%	63.0%		
	Present	Count	0	15	19	3	37		
		%	0.0%	46.9%	35.8%	21.4%	37.0%		
Secretive	Absent	Count	1	26	37	11	75	1.85	0.603
		%	100.0%	81.3%	69.8%	78.6%	75.0%		
	Present	Count	0	6	16	3	25		
		%	0.0%	18.8%	30.2%	21.4%	25.0%		
Polyp	Absent	Count	1	27	43	10	81	1.3	0.72
		%	100.0%	84.4%	81.1%	71.4%	81.0%		
	Present	Count	0	5	10	4	19		
		%	0.0%	15.6%	18.9%	28.6%	19.0%		
Atrophy	Absent	Count	0	30	52	14	96	25.62	0.001*
		%	0.00%	93.80%	98.10%	100.00%	96.00%		
	Present	Count	1	2	1	0	4		
		%	100.00%	6.30%	1.90%	0.00%	4.00%		
Hyperplasia	Absent	Count	1	29	50	13	93	0.49	0.91
		%	100.0%	90.6%	94.3%	92.9%	93.0%		
	Present	Count	0	3	3	1	7		
		%	0.0%	9.4%	5.7%	7.1%	7.0%		
Endometritis	Absent	Count	1	30	50	13	94	0.11	0.99
		%	100.0%	93.8%	94.3%	92.9%	94.0%		
	Present	Count	0	2	3	1	6		
		%	0.0%	6.3%	5.7%	7.1%	6.0%		
EM cancer	Absent	Count	1	32	53	12	98	12.53	0.006*
		%	100.0%	100.0%	100.0%	85.7%	98.0%		
	Present	Count	0	0	0	2	2		
		%	0.0%	0.0%	0.0%	14.3%	2.0%		

*Significant

TVUS findings showed 33% of patients having fibroid, 18% of patients having polyps, and 4% of patients having adenomyosis. No statistically significant association was found between menstrual history and TVUS ($\varkappa 2$= 1.80, p=0.61). (Table 8)

Table 8: Distribution of patients according to menstrual history and TVUS

Menstrual History		TVUS				Total
		Adenomyosis	Fibroid	NAD	Polyp	
Menopause	Count	2	9	18	7	36
	%	50.0%	27.3%	40.0%	38.9%	36.0%
Menstruating	Count	2	24	27	11	64
	%	50.0%	72.7%	60.0%	61.1%	64.0%
Total	Count	4	33	45	18	100
	%	100.0%	100.0%	100.0%	100.0%	100.0%
Chi - square value - 1.80						
p - value - 0.61						

EM thickness of 1 to 4.9 was present in 1 patient who had normal TVUS findings. Around 32 patients had EM thickness between 5 to 9.9, out of which 12 (36.4%) patients had fibroid, and 4 (22.2%) had a polyp. About 53 patients had EM thickness between 10 to 14.9, out of which 18 (54.5%) patients had fibroid, and 10 (55.6%) patients had polyp. Around 14 patients had EM thickness between 15 to 19.9, out of which 3 (9.1%) patients had fibroid, and 4 (22.2%) patients had polyp. No statistically significant association was found between EM thickness and TVUS ($\varkappa 2$= 3.91, p=0.91).

4. Discussion

Abnormal uterine bleeding is the common presenting complaint in Gynaecology Outpatient Department in all age groups. It is due to the anovulatory cycles, which are commonly seen in adolescent and perimenopausal women. Abnormal uterine bleeding is caused by a wide variety of organic and nonorganic causes. Endometrial carcinoma precedes through a spectrum of the disordered proliferative pattern followed by hyperplasia without atypia or hyperplasia with atypia[11]. Sonography followed by histologic assessment remains the cornerstone for diagnosis[12].

Regarding age, 51% of respondents were between the ages of 41 and 50, and 25% were between the ages of 51 and 60. Kumari A et al. found that 44% of women were between 41 to 45 years of age and 39% were more than 50 years of age[13].76% of the 112 perimenopausal women Bhosle investigated were in the 41–45 age range, 2.6% were in the

46–50 age range, and 2.6% were over the age of 51[14]. Cornitescu et al. studied 256 perimenopausal patients and reported 35.5% incidence in the age group of 41–45 years and 64.5% incidence in the age group 46–52 years[15]. According to Kaul et al. study in postmenopausal patients, the mean age of the patient was 54.06 ± 6.64 (41–70), and the mean age at menopause was 47.8 ± 2.82 (range 47–49) [16], whereas according to our study, the mean age of the patients was 47.64 ± 8.56 and the mean age at menopause and the menstruating patient was 56.08 ± 6.67 and 42.89 ± 5.16.

In our study, most of the patients (92%) were multigravida, and 8% were nulli gravida. Sur and Chakravorty found that 75 patients were para 1 - 5, 65 patients were para more than 5, and 23 were nulliparous[17]. Kerala, where there is a high level of acceptability of family planning practises, is where Pillai SS did his study. Thus, 7.45% of patients had para 2 or less, 25% had para 2 or more, and 4.5% had nulliparous pregnancies[7].

Menorrhagia, which was present in 54% of patients in the current study, was followed by post - menstrual bleeding (PMB), which was present in 34% of patients, polymenorrhoea, which was present in 8% of patients, and post - coital bleeding, which was present in 4% of patients These findings are similar to those of the Pillai SS study, in which menorrhagia was the most frequent clinical presentation seen in 46.5% of cases, following with menometrorrhagia at 21.5%[7].

Endometrial thickness was assessed using ultrasonography. In our study, the mean EM thickness based on menstrual history was 10.58 ± 3.89 in menopause patients and 11.22 ± 3.03 in menstruating patients. The EM thickness was in the range of 10 to 14.9 in 53% of patients, 32% of patients had an EM thickness between 5 to 9.9, 14% of patients had an EM thickness in the range of 15 to 19.9 and only 1% patient had EM thickness between 1 to 4.9. In Sujana G et al. In the study, the majority of the patients (46.86%) had endometrial thickness between 5 and 10 mm, followed by 11 to 15 mm in 39.01%[18]. Studies by Shrestha et al. and Sur & Chakravorty had the majority of patients in the endometrial thickness range of 11 - 15mm (48.57% and 42.07%) followed by 5 - 10mm (35.24% and 32.32%) [18, 19]. According to Pillai SS, 46.6% of the 88 patients had endometrial thicknesses between 5 and 9.9 mm, or 41 out of the 88 individuals. In between 10 and 14.9 mm, endometrial thickness was present in about 22.7% of individuals[7].

Evaluation of histopathological features and menstrual history found that the proliferative features were present in 37% of patients, about 8% in menopause patients, and 29% in menstruating patients. Secretive histopathological feature was seen in 25% of patients, polyp was seen in 19% of patients, atrophy was seen in 4% of patients in the menopause group, hyperplasia was seen in 7%, endometritis was present in 6%, EM cancer was seen in 2% of menopause patients. This is in contrast to the study of Sujana G et al., atrophic endometrium was reported in 0.26% of patients[18]. Shreshtha et al. found 1.9%, Sur & Chakravorthy found 1.82%, and Pillai SS found 1.13%[7, 18, 19]. Sur & Chakravorthy, Pillai SS, and Das et al. reported a much higher incidence of proliferative endometrium[7, 18, 20].

24 patients were found to have proliferative endometrial according to the Pillai SS study, while 20 patients were found to have disordered proliferative endometrium. Although 17 patients had hyperplastic modifications, only 5 of them had complicated hyperplasia with atypia. In 4 cases, endometrial adenocarcinoma was discovered. The most frequent histology pattern was proliferative endometrium. In 22.7% of the patients, disordered proliferation was discovered, which is thought to be an intermediate stage between endometrial hyperplasia and normal proliferative endometrium[7].

In our study, atrophy was present in 4% of patients; 1% of each had an EM thickness between 1 to 4.9, 10 to 14.9, and 2% of patients had an EM thickness between 5 to 9.9. EM cancer was present in 2% of patients having a thickness of 15 to 19.9. In the study by Sujana et al., atropic endometrium was reported in 1.57% of patients with EM thickness < 5mm[18]. Das et al. study reported 1%[20]. Sujana et al. reported with a thickness range of 11 - 15mm, 0.52% had carcinoma[18]. Carcinoma was seen in 0.95% of cases of the study done by Shrestha et al., which is less incidence compared to our study[19]. With the increase in the endometrial thickness from 15 to 19.9 mm, we observed that there is an increase in the cases of endometrial carcinoma. This is similar to the study of Sujana et al. reported that with the increase in the endometrial thickness from < 5mm to >20 mm, there is an increase in the patients with endometrial carcinoma[18]. According to Getpook et al study, perimenopausal women with abnormal uterine bleeding are less likely to have malignant pathology when their endometrial thickness is 8 mm perimenopausal despite prolonged bleeding or less[21]. An EM thickness of 4 mm or less in post - menopausal women is regarded as normal; anything beyond that increases the risk of abnormalities including hyperplasia and cancer. In perimenopausal women, there is no consensus on what constitutes abnormal endometrial thickness. Although there is disagreement over the top limit for normal endometrial thickness, the majority of studies have identified transvaginal sonographic endometrial thickness of 8 mm perimenopausal despite prolonged bleeding as the abnormal cut - off value, calling for additional research[22].

TVUS findings showed 33% of patients having fibroid, 18% of patients having polyps, and 4% of patients having adenomyosis. The endometrial polyp was reported in 0.26% of cases in the study of Sujana et al. [Sujana et al 2020] EM thickness of 1 to 4.9 was present in 1 patient who had normal TVUS findings.32 patients had EM thickness between 5 to 9.9, out of which 12 (36.4%) patients had fibroid, and 4 (22.2%) had polyp. Around 53 patients had EM thickness between 10 to 14.9, out of which 18 (54.5%) patients had fibroid, and 10 (55.6%) patients had polyp. Around 14 patients had EM thickness between 15 to 19.9, out of which 3 (9.1%) patients had fibroid, and 4 (22.2%) patients had polyp. This is similar to the study done by Pillai SS, i. e., 55.7% and 7.9% of patients who had fibroid uteri at the time of the patient's presentation had endometrial polyps as the root cause[7].

5. Conclusion

Since it is comparatively inexpensive, secure, and non - invasive, transvaginal ultrasonography (TVUS) is the recommended first - line diagnostic method. It will show additional pelvic pathologies in addition to endometrial thickening. In cases of The primary indication for further evaluation for invasive methods like hysteroscopy and DD&C, should be reserved for cases with documented abnormal endometrium thickness ≥ 8 mm in perimenopausal women and ≥ 5 mm in postmenopausal women or heterogeneous structural pattern on TVUS suspicious of malignancy inconclusive TVUS, endometrial tissue should be obtained in order to screen out precancerous lesions or endometrial cancer as the primary indication for invasive treatments like D&C

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